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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,046	04/01/2005	Yukiko Yokoi	2005_0520A	7940

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EXAMINER	
HOUGHTLING, RICHARD A	

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1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,046	YOKOI ET AL.	
	Examiner	Art Unit	
	RICHARD A. HOUGHTLING	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *27-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-30 are pending in this application. The Examiner acknowledges receipt of Applicant's response to the restriction requirement filed on 15 February in which applicant elected Group I corresponding to claims 1-26, without traverse. Applicant further elected hydroxypropylmethyl cellulose as the species of water-soluble high polymer; and thus, the **restriction requirement is MADE FINAL**. Claims 27-30 are withdrawn from further consideration as they pertain to non-elected groups; therefore, claims 1-26 are pending and examined on their merits herein.

Priority

2. Applicants' claim to foreign priority to JP2002-290367 corresponding to a priority date of 02 October 2002 is acknowledged and entered in the record.

Information Disclosure Statements

3. Receipt of four information disclosure statements filed by applicants on 01 April 2005; 15 July 2005; 20 August 2007 and 10 September 2007 is acknowledged; examiner entered the disclosures into the record and references were considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2, 5 and 9-11 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 5 and 9-11 recite the limitation "100 mg efficacy" of cefditoren pivoxil in the pharmaceutical composition found in claim 1. Efficacy is a relative term, and it is unclear from the specification as to which effect of the drug the 100 mg efficacy pertains.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimizu et al. (WO00/06126, see PTO-892) and Onodera et al. (U.S. Patent 6,486,149 as found in Applicants' IDS received on 10 September 2007), and further in view of Sigma-Aldrich catalog entry for Tween 80 (see PTO-892, Reference U).

Shimizu et al. teach a rapidly disintegrable solid pharmaceutical preparation comprising a pharmacologically active ingredient of which the antibiotic, cefditoren pivoxil, is included within a Markush group (see p. 7, line 8); a polymer, for example, hydroxypropylmethylcellulose (see p. 12, line 25; p. 17, lines 18-20 and 27; and p. 32 Example 1, in Table corresponding to the "Undercoating Liquid"); and a sugar ester fatty acid (Polysorbate 80, also known as sorbitan monooleate, see p. 33 Table corresponding to the "Enteric film coating liquid").

The pharmaceutical preparations taught by Shimizu et al. thus comprise each and every essential ingredient of Applicant's invention including cefditoren pivoxil and a sugar ester fatty acid (sorbitan monooleate, see p. 33). Applicant's invention also may further comprise a pharmaceutically acceptable polymer (claim 3) which is also represented as a water-soluble high polymer (claim 8) and is hydroxypropylmethyl cellulose (claim 4). Each of these additional limitations are also taught by Shimizu et al., in that the polymer—hydroxypropylmethyl cellulose is included in the undercoating liquid (see p. 32, lines 18-20). Further Applicant's invention may also comprise one or more pharmaceutically acceptable additives (claims 6 and 12-16); which are likewise taught by Shimizu et al. as being included in the initial inner core (Spray liquid) which contains the pharmacologically active agent, as well as magnesium carbonate, a well-established pharmaceutically acceptable additive or the inclusion of triethyl citrate or glyceryl monostereate (see Table on p. 33, "Enteric film coating liquid").

Applicant's pharmaceutical composition is further defined in that it comprises particles of cefditoren pivoxil present in an interior portion of said particles and a sugar ester fatty acid present in an exterior portion of said particles (claim 20). In Example 1, Shimizu et al. teach production of powders having a core in which the active pharmacological ingredient (herein Lansoprazole) is found in the initial spray liquid in the presence of low-substituted hydroxypropyl cellulose and hydroxypropyl cellulose resulting in a powder with a core containing the active pharmacological agent. A second coating is made using an undercoating liquid (see p. 32) using hydroxypropylmethyl cellulose and purified water. This layer is then coated using an enteric film coating liquid which contains the sorbitan monooleate (i.e., the sugar ester fatty acid, Polysorbate 80, see Table p. 33). Thus, in this example, the active pharmacological ingredient is the interior portion of the particles and the sugar ester fatty acid is located on the exterior portion of these particles. Similar to the pharmaceutical composition of claim 1, the composition of claim 20 also further comprises a pharmaceutically acceptable polymer (claim 23), which is hydroxypropylmethyl cellulose (claim 24). As stated above, these additional components are taught by Shimizu et al. (see p. 32, Tables for Spray liquid, lines 8-10 or Undercoating liquid, lines 18-20). Applicant further claims that the pharmaceutical may be produced as a tableted dose form which is also disclosed by Shimizu et al. in section (7) production of orally disintegrable tablets that result in individual tablets each weighing 500 mg.

Applicant's invention further limits the amount of sugar ester fatty acid (0.1 mg-100 mg) or the amount of the polymer (1-100 mg) relative to the amount of cefditoren pivoxil (100 mg efficacy). The adjustment of particular conventional working conditions (e.g., determining result effective amounts of the ingredients beneficially taught by the cited reference, especially within the broad ranges instantly claimed), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. Accordingly, this type of modification would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Shimizu et al. does not teach amorphous cefditoren pivoxil or the inherent property of the hydrophile-lipophile balance (HLB) value of sorbitan monooleate (TWEEN 80).

Onodera et al. teach a process of making amorphous cefditoren pivoxil. Onodera et al. disclosed that orthorhombic crystalline Cefditoren pivoxil had several advantages of high purity, high thermal stability and high storage stability, but that it was unsuitable for use in an oral dosage form due to its poor water solubility (see col. 2, lines 44-50). To overcome this poor water solubility, Onodera et al. teach that, "it is known that an amorphous substance generally has a high solubility in water, as compared with that of the corresponding crystalline substance" (see col. 2, lines 60-66). Onodera et al. further teach that an orally administrable amorphous and water soluble substance of Cefditoren pivoxil is obtained when Cefditoren pivaloyloxymethyl ester is

homogenously mixed with a water-soluble high-molecular additive such as a water-solubilized derivative of hydroxypropylmethyl cellulose and a pharmaceutically acceptable alkali metal salt or alkaline earth metal salt of an alginic acid ester of propylene glycol (see col. 3, lines 46-59; col. 6, lines 48-67 to col. 7, lines 1-43; col. 15 Example 2, wherein hydroxypropylmethyl cellulose is used; and Example 7 spanning col. 20-21).

Because the amorphous Cefditoren pivoxil taught by Onodera et al. has about 10-fold greater water solubility (see results in Test Example 1, col. 27, lines 7-38 wherein the orthorhombic crystalline substance had a water solubility of about 0.4 mg/ml compared to the results of the compound obtained in Example 6 which had a water solubility of about 4 mg/ml); it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to employ the amorphous Cefditoren pivoxil taught by Onodera et al. into the pharmaceutical taught by Shimizu et al. in order to improve the water solubility of the cefditoren pivoxil and improve its overall absorption and efficacy.

The product information sheet for TWEEN-80 as found at http://www.sigmaaldrich.com is relied upon for its reference to the HLB value of 15.0 for sorbitan monooleate.

Thus the pharmaceutical composition as taught by Shimizu et al. further meets Applicant's limitations to use of a sugar ester fatty acid with an HLB value of greater than 10 (claim 21) and also wherein the sugar ester fatty acid has an HLB value within the range of 11-20. Because the product information sheet discloses that sorbitan monooleate has an HLB value of 15.0; therefore, each and every limitation of claims 21 and 22 are met by the pharmaceutical composition taught by Shimizu et al.

It would have been obvious at the time of applicant's invention to one of ordinary skill in the art to select cefditoren pivoxil from the Markush group listing on p.7 and employ the coating techniques found in Example 1, substituting cefditoren pivoxil for the Lansoprazole would be reasonably expected to achieve a predictable result as that described in Example 1.

Conclusion

6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard A. Houghtling whose telephone number is (571) 272-9334. The examiner may normally be reached Mon-Thurs 8:30 am - 5:00 pm and alternate Fridays 8:30 am - 12:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan may be reached on (571) 272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard A. Houghtling, Ph.D.
Patent Examiner

/San-ming Hui/
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